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* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	OCT 04	Removal of Pre-IPC 8 data fields streamlines displays in USPATFULL, USPAT2, and USPATOLD.
NEWS	3	OCT 04	Precision of EMBASE searching enhanced with new chemical name field
NEWS	4	OCT 06	Increase your retrieval consistency with new formats or for Taiwanese application numbers in CA/CAPLUS.
NEWS	5	OCT 21	CA/CAPLUS kind code changes for Chinese patents increase consistency, save time
NEWS	6	OCT 22	New version of STN Viewer preserves custom highlighting of terms when patent documents are saved in .rtf format
NEWS	7	OCT 28	INPADOCDB/INPAFAMDB: Enhancements to the US national patent classification.
NEWS	8	NOV 03	New format for Korean patent application numbers in CA/CAPLUS increases consistency, saves time.
NEWS	9	NOV 04	Selected STN databases scheduled for removal on December 31, 2010
NEWS	10	NOV 18	PROUSDDR and SYNTHLINE Scheduled for Removal December 31, 2010 by Request of Prous Science
NEWS	11	NOV 22	Higher System Limits Increase the Power of STN Substance-Based Searching
NEWS	12	NOV 22	Enjoy a free month of INPADOCDB/INPAFAMDB SDIs!
NEWS	13	NOV 24	Search an additional 46,850 records with MEDLINE backfile extension to 1946
NEWS	14	DEC 14	New PNK Field Allows More Precise Crossover among STN Patent Databases
NEWS	15	DEC 18	ReaxysFile available on STN
NEWS	16	DEC 21	CAS Learning Solutions -- a new online training experience
NEWS	17	DEC 22	Value-Added Indexing Improves Access to World Traditional Medicine Patents in CAPLUS

NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
AND CURRENT DISCOVER FILE IS DATED 07 JULY 2010.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 09:27:23 ON 10 JAN 2011

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.23	0.23

FILE 'REGISTRY' ENTERED AT 09:27:33 ON 10 JAN 2011

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STRUCTURE FILE UPDATES: 9 JAN 2011 HIGHEST RN 1258835-38-9

DICTIONARY FILE UPDATES: 9 JAN 2011 HIGHEST RN 1258835-38-9

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2010.

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=> s carboxypeptidase G2

3268 CARBOXYPEPTIDASE

8397 G2

L1 44 CARBOXYPEPTIDASE G2

(CARBOXYPEPTIDASE(W)G2)

=> s raltitrexed

L2 1 RALTITREXED

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	17.61	17.84

FILE 'CAPLUS' ENTERED AT 09:27:52 ON 10 JAN 2011

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FILE COVERS 1907 - 10 Jan 2011 VOL 154 ISS 3
FILE LAST UPDATED: 9 Jan 2011 (20110109/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2010

CAPLUS now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2010.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l1 and l2
      29 L1
      887 L2
L3      0 L1 AND L2
```

```
=> fil medline embase biosis
COST IN U.S. DOLLARS                               SINCE FILE      TOTAL
                                                    ENTRY      SESSION
FULL ESTIMATED COST                               0.52      18.36
```

FILE 'MEDLINE' ENTERED AT 09:28:10 ON 10 JAN 2011

FILE 'EMBASE' ENTERED AT 09:28:10 ON 10 JAN 2011
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FILE 'BIOSIS' ENTERED AT 09:28:10 ON 10 JAN 2011
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```
=> s carboxypeptidase
L4      114247 CARBOXYPEPTIDASE
```

```
=> s raltitrexed
L5      2728 RALTITREXED
```

```
=> s l4 and l5
L6      8 L4 AND L5
```

```
=> dup rem l6
PROCESSING COMPLETED FOR L6
L7      6 DUP REM L6 (2 DUPLICATES REMOVED)
```

```
=> d l7 1-6 ibib abs
```

L7 ANSWER 1 OF 6 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007601995 EMBASE
TITLE: Multidrug resistance associated proteins as determining factors of pharmacokinetics and pharmacodynamics of drugs.
AUTHOR: Yu, Xue-Qing (correspondence)
CORPORATE SOURCE: Department of Nephrology, Sun Yat-sen University, Guangzhou 510080, China. yuxq@mail.sysu.edu.cn
AUTHOR: Xue, Charlie Changli
CORPORATE SOURCE: The RMIT Chinese Medicine Research Group, Division of

Chinese Medicine, RMIT University, Melbourne, VIC,
Australia.

AUTHOR: Wang, Guangji
CORPORATE SOURCE: Key Lab. of Drug Metabolism and Pharmacokinetics, China
Pharmaceutical University, 1 Shennong Road, Nanjing 210038,
China.

AUTHOR: Zhou, Shu-Feng
CORPORATE SOURCE: Division of Pharmacy, School of Life Sciences, Queensland
University of Technology, 2 George Street, Brisbane, QLD
4001, Australia. s4.zhou@qut.edu.au

SOURCE: Current Drug Metabolism, (Dec 2007) Vol. 8, No. 8, pp.
787-802.
Refs: 262
ISSN: 1389-2002 CODEN: CDMUBU

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 022 Human Genetics
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 10 Jan 2008
Last Updated on STN: 10 Jan 2008

AB The multidrug resistance associated proteins (MRP1, MRP2, MRP3, MRP4, MRP5, MRP6, MRP7, MRP8 and MRP9) belong to the ATP-binding cassette superfamily (ABCC family) of transporters. They are expressed differentially in the liver, kidney, intestine, brain and other tissues. These transporters are localized to the apical and/or basolateral membrane of the hepatocytes, enterocytes, renal proximal tubule cells and endothelial cells of the blood-brain barrier. Several MRPs (mainly MRP1-3) are associated with tumor resistance which is often caused by an increased efflux and decreased intracellular accumulation of natural product anticancer drugs and other anticancer agents. MRPs transport a structurally diverse array of important endogenous substances and xenobiotics and their metabolites (in particular conjugates) with different substrate specificity and transport kinetics. Most MRPs are subject to induction and inhibition by a variety of compounds. Several nuclear receptors, including pregnane X receptor (PXR), liver X receptor (LXR), and farnesoid receptor (FXR) participate in the regulation of MRPs. MRPs play an important role in the absorption, distribution and elimination of various drugs in the body and thus may affect their efficacy and toxicity and cause drug-drug interactions. MRPs located in the blood-brain barrier can restrict the penetration of compounds into the central nervous system. Mutation of MRP2 causes Dubin-Johnson syndrome, while mutations in MRP6 are responsible for pseudoxanthoma elasticum. More recently, mutations in mouse Mrkp6/Abcc6 gene is associated with dystrophic cardiac calcification (DCC), a disease characterized by hydroxyapatite deposition in necrotic myocytes. A single nucleotide polymorphism, 538G>A in the MRP8/ABCC11 gene, is responsible for determination of earwax type. A better understanding of the function and regulating mechanism of MRPs can help minimize and avoid drug toxicity, unfavourable drug-drug interactions, and to overcome drug resistance.
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L7 ANSWER 2 OF 6 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006507619 EMBASE
TITLE: Gamma-glutamyl hydrolase and drug resistance.
AUTHOR: Schneider, Erasmus (correspondence); Ryan, Thomas J.

CORPORATE SOURCE: Wadsworth Center, New York State Department of Health,
Department of Biomedical Sciences, University at Albany,
Empire State Plaza, Albany, NY 12201, United States.
schneid@wadsworth.org

SOURCE: Clinica Chimica Acta, (Dec 2006) Vol. 374, No. 1-2, pp.
25-32.

Refs: 85

ISSN: 0009-8981 CODEN: CCATAR

PUBLISHER IDENT.: S 0009-8981(06)00375-5

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 022 Human Genetics
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 9 Nov 2006

Last Updated on STN: 9 Nov 2006

AB Gamma-glutamyl hydrolase (GGH) is a lysosomal enzyme involved in the metabolism of folates and anti-folates. It acts as an endo- and/or exo-peptidase to cleave gamma-polyglutamate chains that are attached to folates and anti-folates after they enter a mammalian cell. Whereas the addition of multiple glutamates is necessary to enable the cell to retain folates and anti-folates, hydrolysis of the polyglutamate tails by GGH has the opposite effect of making (anti)-folates exportable again. Thus, GGH plays an important role in the cellular homeostasis of folate. Furthermore, high levels of GGH have been associated with cellular resistance to anti-folates, in particular methotrexate. Consequently, GGH also has pharmacological importance. In addition to the intracellular GGH, carboxypeptidase II (also called intestinal folate conjugase, prostate specific membrane antigen or N-acetyl- α -linked acidic dipeptidase) is another enzyme with γ -glutamyl hydrolase activity; it resides, however, in the cellular membrane. Although genetically and biochemically distinct, this enzyme too appears to play a major role in folate homeostasis, by cleaving polyglutamates from extracellular folate-polyglutamates, so that they can be imported into the cell. Finally, there have been reports suggesting that γ -glutamyl hydrolase plays a role as a tumor marker in breast and lung cancer.
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ACCESSION NUMBER: 2004033045 EMBASE

TITLE: [Renal, hepatic, biliary, and cardiovascular emergencies in onco-haematology].
Urgences renales, hepato-biliaires et cardiaques en oncohematologie.

AUTHOR: Nitenberg, Gerard (correspondence); Blot, Francois;
Raynard, Bruno

CORPORATE SOURCE: Serv. de Reanimation Medico-Chir., Institut Gustave Roussy,
94805 Villejuif Cedex, France. nitenber@igr.fr

SOURCE: Revue du Praticien, (15 Dec 2003) Vol. 53, No. 19, pp.
2160-2170.

Refs: 28

ISSN: 0035-2640 CODEN: REPRA3

COUNTRY: France

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: French

SUMMARY LANGUAGE: English; French

ENTRY DATE: Entered STN: 12 Feb 2004

Last Updated on STN: 12 Feb 2004

AB Whether they are the first sign of cancer or aggravate the evolution of a neoplasm already known and treated, renal, hepatic and cardiac failure constitute a vital threat for a patient with cancer and often justifies an admission to intensive care. If the clinical picture can be considered similar in all respects to that of other patients, the neoplasia and its treatments are often responsible for etiological, diagnostic, prognostic and therapeutic particularities that merit being known. So it is in nephrology with the glomerulopathies and thrombotic microangiopathy, in hepatology with veno-occlusive disease and graft versus host rejection, in cardiology with aplastic septic shock, anthracycline myocardial toxicity, cardiac tamponade... the list is far from being exhaustive. We have attempted to clarify certain of these specificities and the diagnostic and therapeutic approach adapted to these situations that are too often the source of errors with serious consequences.

L7 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 1997175090 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9022750

TITLE: Prodrugs of thymidylate synthase inhibitors: potential for antibody directed enzyme prodrug therapy (ADEPT).

AUTHOR: Springer C J; Bavetsias V; Jackman A L; Boyle F T; Marshall D; Pedley R B; Bisset G M

CORPORATE SOURCE: CRC Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton, Surrey, UK.

SOURCE: Anti-cancer drug design, (1996 Dec) Vol. 11, No. 8, pp. 625-36.

Journal code: 8603523. ISSN: 0266-9536. L-ISSN: 0266-9536.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 6 Mar 1997

Last Updated on STN: 3 Mar 2000

Entered Medline: 27 Feb 1997

AB Prodrugs of quinazoline antifolate thymidylate synthase (TS) inhibitors have been designed and synthesized for use in antibody-directed enzyme prodrug therapy (ADEPT). The syntheses of the alpha-linked dipeptides of two potent thymidylate synthase inhibitors, ZD1694 [N-[5-[N-(3,4-dihydro-2-methyl-4-oxoquinazolin-6-ylmethyl)-N-methylamino]-2-thenoyl]-L-glutamic acid] and ICI198583 N-[4-[N-[(2-methyl-3,4-dihydro-4-oxo-6-quinazolinyl) methyl]-N-prop-2-ynylamino]benzoyl]-L-glutamic acid are described. The alpha-carboxyl of the glutamic acid has been linked through an amide bond to an L-alanine or an L-glutamic acid. The alpha-linked L-dipeptide prodrugs were designed to be activated to their corresponding thymidylate synthase inhibitors at a tumour site by prior administration of a monoclonal antibody conjugated to the enzyme carboxypeptidase A (CPA). The viability of a colorectal cell line was monitored with the potential prodrugs in the presence or absence of CPA or with the parent drugs alone. All the dipeptides had greatly decreased cytotoxicity, with a deactivation of approximately 100-fold for the ZD1694 prodrugs and approximately 20-200-fold for the ICI198583 prodrugs. Activation of the alpha-linked L-alanine dipeptides with CPA led to a cytotoxicity enhancement of approximately 10-100 fold.

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ACCESSION NUMBER: 1994064029 EMBASE

TITLE: Enzymatic synthesis of folate and antifolate polyglutamates with Escherichia coli folylpolyglutamate synthetase.
AUTHOR: Hanlon, M.H. (correspondence); Ferone, R.; Weaver, K.; Ray, P.
CORPORATE SOURCE: Wellcome Res. Labs., Dept. Molec. Genet. and Microbiol., Res Triangle Pk, NC 27709, United States.
AUTHOR: Hanlon, M.H. (correspondence)
CORPORATE SOURCE: Molecular Genetics/Microbiol. Dept., Wellcome Research Laboratories, Research Triangle Park, NC 27709, United States.
SOURCE: Analytical Biochemistry, (1994) Vol. 216, No. 2, pp. 345-351.
ISSN: 0003-2697 CODEN: ANBCA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Apr 1994
Last Updated on STN: 6 Apr 1994

AB Escherichia coli folylpolyglutamate synthetase was used to synthesize micromole quantities of polyglutamyl conjugates of folic acid, methotrexate, and other analogs of folic acid. The products of the enzymatic reactions were purified by semipreparative C18 HPLC. The position of each amide linkage (γ or α carboxyl) in the polyglutamated products was determined by limited and exhaustive hydrolyses with hog kidney folylpolyglutamate hydrolase and with yeast carboxypeptidase Y. Under standard reaction conditions, the E. coli enzyme added up to five glutamyl residues to each monoglutamated substrate, primarily at the γ carboxyl position. Thus, an enzyme which naturally adds only two glutamates to naturally occurring folates can be used synthetically to make higher polyglutamates of a wide range of synthetic substrates. The products of the reactions are valuable tools for the study of the metabolism of antifolate drugs as well as metabolic reactions involving folate cofactors.

L7 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1992194266 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1372358
TITLE: Syntheses and thymidylate synthase inhibitory activity of the poly-gamma-glutamyl conjugates of N-[5-[N-(3,4-dihydro-2-methyl-4-oxoquinazolin-6-ylmethyl)-N-methylamino]-2-thenoyl]-L-glutamic acid (ICI D1694) and other quinazoline antifolates.
AUTHOR: Bisset G M; Pawelczak K; Jackman A L; Calvert A H; Hughes L R
CORPORATE SOURCE: Institute of Cancer Research, Cancer Research Campaign Laboratories, Sutton, Surrey, England.
SOURCE: Journal of medicinal chemistry, (1992 Mar 6) Vol. 35, No. 5, pp. 859-66.
Journal code: 9716531. ISSN: 0022-2623. L-ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 6 Feb 1998
Entered Medline: 17 Apr 1992

AB Thirteen poly-gamma-glutamates derived from several novel antifolates have been synthesized by a convergent route. The syntheses of poly-gamma-glutamyl conjugates of N-[5-[N-(3,4-dihydro-2-methyl-4-oxoquinazolin-6-ylmethyl)-N-methylamino]-2-theno yl]-L-glutamic acid (8) (ICI D1694), 2-desamino-N10-propargyl-5,8-dideazafolic acid (6), 2-desamino-2-methyl-N10-propargyl-5,8-dideazafolic acid (7), 2-desamino-2-methyl-N10-propargyl-2'-fluoro-5,8-dideazafolic acid (9), and 2-desamino-2-methyl-4-chloro-N10-propargyl-2'-fluoro-3,5,8-trideazafo lic acid (11) are described. A key step in the route involves coupling of an alpha-tert-butyl-protected poly-gamma-glutamate of the required chain length to the appropriate 5,8-dideazapteroic acid, obtained by carboxypeptidase G2 cleavage of the parent monoglutamate, if available, or by chemical synthesis. Deprotection with trifluoroacetic acid in the final step gave the desired poly-gamma-glutamyl antifolates as their trifluoroacetate salts. As inhibitors of thymidylate synthase, these polyglutamates were more potent in every case than the corresponding non-polyglutamylated drug.

=> d his

(FILE 'HOME' ENTERED AT 09:27:23 ON 10 JAN 2011)

FILE 'REGISTRY' ENTERED AT 09:27:33 ON 10 JAN 2011

L1 44 S CARBOXYPEPTIDASE G2

L2 1 S RALTITREXED

FILE 'CAPLUS' ENTERED AT 09:27:52 ON 10 JAN 2011

L3 0 S L1 AND L2

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 09:28:10 ON 10 JAN 2011

L4 114247 S CARBOXYPEPTIDASE

L5 2728 S RALTITREXED

L6 8 S L4 AND L5

L7 6 DUP REM L6 (2 DUPLICATES REMOVED)

=> s l4 and methotrexate

L8 1319 L4 AND METHOTREXATE

=> d his

(FILE 'HOME' ENTERED AT 09:27:23 ON 10 JAN 2011)

FILE 'REGISTRY' ENTERED AT 09:27:33 ON 10 JAN 2011

L1 44 S CARBOXYPEPTIDASE G2

L2 1 S RALTITREXED

FILE 'CAPLUS' ENTERED AT 09:27:52 ON 10 JAN 2011

L3 0 S L1 AND L2

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 09:28:10 ON 10 JAN 2011

L4 114247 S CARBOXYPEPTIDASE

L5 2728 S RALTITREXED

L6 8 S L4 AND L5

L7 6 DUP REM L6 (2 DUPLICATES REMOVED)

L8 1319 S L4 AND METHOTREXATE

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	21.50	39.86

STN INTERNATIONAL LOGOFF AT 09:29:39 ON 10 JAN 2011